

Supporting Information for

Thermoring switch for TRPV2 inactivation

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This supplementary material includes:

Table S1: Tertiary noncovalent interactions in 2-APB-activated rTRPV2 at 4 °C (PDB ID: 7N0N).

Table S2: Tertiary noncovalent interactions in 2-APB-inactivated rTRPV2 at 4 °C (PDB ID: 7N0M).

Table S3: Tertiary noncovalent interactions in 2-APB/CBD-activated rTRPV2 at 4 °C (PDB ID: 7T37).

Table S4: Tertiary noncovalent interactions in 2-APB/CBD-inactivated rTRPV2 at 4 °C (PDB ID: 7T38).

Table S5: Tertiary noncovalent interactions in 2-APB-PBC-activated rTRPV2 at 4 °C (PDB ID: 9B3V).

Table S1. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 2-APB-activated rTRPV2 in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID: 7N0N).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	R328-D344, D349-R684, E358-R459-E670, R369-D469, R388-E685, K531-E647
H-bond	<3.9 Å donor-H-acceptor <60°	V254/M255-K307, D258-S260, Y271-E288-R317, N292-L296, Q294-K304, T297- K300-N354 , K304-C364, G306-N368, Q316-Y343, E318-Q324, S327-R702, R328-S346, K329-Y343/D344, E332-R706, D344-S346-S347, S350-E672, S355-E358, S366-N368, H370-S658, K385-L381, Y403-Q479, Q452-E473, R458-E670, S466-S470, S486/R490-Y497, Y514-S667, I524-S656, S526-Q530, Y544-T604-Y629, Y544-Y629, S559-P589, E672-R680, N673-R679
π - π interaction	2.65–6.5 Å	W333-Y335, F362-F462, W386-F393-Y515, F394-F519, F397-Y515, Y400-Y403-Y407, Y400-F476, Y400-Y515, Y412-H413, H438-F491, Y447-Y675/W676, W454-W457, W454-W676, Y455-F456, Y471-F472-Y514, F476-Y514/Y515, Y514-Y515, F540-Y544, Y544-F601, F551-Y629, W657-W660, W676-W677, W712-W715
cation- π interaction	<6.0 Å	W351-R684-W703, F362-R459, W386-K664, R684-W703, R388-H683, W457-R460
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, Q276-Y323, F330-V691, W333-V340, Y343-P377, P337-W712/W715, L381-F705, W386-V390, F405-V409, I463-W464, Y497-L498, F540-M640, L600-Y629-T633, W657-K661, W660-K664, L688-W703, W715-L719
Lone pair- π interaction	3-3.7 Å	Q276-F319, F311-M372, F429-S432, Y455-E473

Table S2. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 2-APB-inactivated rTRPV2 in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID: 7N0M).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	E288-R317, E309-R312, E332-R687, D349-R684, R369-D469, K385-E685, E561-R617, E599-K602, R706-E708
H-bond	<3.9 Å donor-H-acceptor <60°	M255-K307, D258-N263, N259-N368, Y271-E288, D272-H313, R280-Y323, N292-L296, A303/K304-C364, G306-N368, Q316-E376, R317-L326/S327/R328/K329, P325/S327-R702, R328-S346, T331-L722, E332-S723-T721, D344-S346/R702, N368-R371, H370-S658, N396-Y675, Y400-G508, T408-W509, Q414-H438, Y447-W677, Q452-E473, S466-D469, M468-Q530, Q479-S504, L475-N511, Q487-R490, Y544-T604/Y629, R563-Q615, S592-D595, L600-Y629, H651-S656, G692-D700
π - π interaction	2.65–6.5 Å	F362-F462, W386-F393-Y515, F394-F519, F397-Y515, Y400-Y403-F407, Y400-F476, Y400-Y515, Y412-H413, Y447-W676, W454-W457/W676, Y455-F456, F467-Y471, F472-F476, F472-Y514, F476-Y514/Y515, Y514-Y515, F540-Y544-F601, F551-Y629, F603-Y629, W657-W660, W676-W677, W712-W715
cation- π interaction	<6.0 Å	F362-R459, W386-K664, R392-Y675, H438-R490, W454-R458, W457-R460, R684-W703
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, Q276-Y323, K329-Y343, F330-V691, W333-P726, P337-W712, W351-R684, L381-F705, M404-W509, H438-V410, Y455-R459, R490-Y497, V543-F547, Y544-L548, F549-V553, L555-Y590, P589-Y590, R617-F618, W657-K661, L688-W703
Lone pair- π interaction	3-3.7 Å	Q276-F319, F476-N511, Y629-T633, W677-C678

Table S3. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 2-APB/CBD-activated rTRPV2 in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID: 7T37).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	E332-R706, D344-R702, R369-D469, R388-E685, R459-E670, E672-K682
H-bond	<3.9 Å donor-H-acceptor <60°	I256-N263, D258-S260, Y271-E288-R317, D272-H313, N292-L296, K300-N354 , K304-H363/C364, R317-L326/R328/K329, F319/Q324-S327, S327-R702, R328-S346-S347-E352, D349-S355/R684, S350-K385/K682, L353-S355-E685, A361-R369, S366-N368, Q383-K661, E384-R388, H438-Q487, R458-E670, T483-S504, T516-T522, Y544-T604/Y629, E561-R617, R563-Q615, E599-K602, L600-Y629, K690-G692
π - π interaction	2.65–6.5 Å	F330-Y343, W386-F393-Y515, F393-F394-F519-F397-Y515, Y400-Y403, Y400-F476, Y400-Y515, Y412-H413, Y447-W676/W677, W454-W457, Y455-F456, Y471-F472-Y514, F476-Y514/Y515, Y514-Y515, Y544-F601, F547-F551, F547/F551-Y629, W657-W660, W676-W677, W712-W715
cation- π interaction	<6.0 Å	W351-R684-W703, F362-R459, W386-K664, R392-Y675, W457-R460, R490-Y497
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, Q276-Y323, K329-Y343, F330-V691, W333-V340, P337-W712, H370-I659, W386-V390, M404-W509, W454-W676, Y455-R459, I524-W660, F540-Y544/M640, F547-L636, F549-V553, F612-L623, R617-F618, W657-K661, L688-W703, W715-L719
Lone pair- π interaction	3-3.7 Å	Q276-F319, Y447-W675, F467-S470, F476-N511, Y629-T633

Table S4. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 2-APB/CBD-inactivated rTRPV2 in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID: 7T38).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	E305-K307, R328-D344, E332-R687, R459-E473
H-bond	<3.9 Å donor-H-acceptor <60°	M255-K307, D258-N263, Y271-E288, D272-H313, N292-L296, A303/K304-C364, E309-R312, Q316-E376, R317-L326/S327/R328, R328-S346-D344, T331-T721, D349-R684, S366-N368, N368-R371, R392-M671, F429-S432, Q414-H438-Q487, Y455-R458/E473, S470-E473, T516-F519/T522, R517-W660, I524-S656, R535-R539, Y544-T604-F601, R563-Q615, E599-K602, D700-R702-C704-R687
π - π interaction	2.65–6.5 Å	W386-F393-Y515, F394-F519, F397-Y515/F519, Y400-Y403-F407, Y400-F476, Y400-Y515, Y412-H413, Y447-W676/W677, W454-W457/W676, Y455-F456, Y471-F472, F472-Y514, F476-Y514/Y515, Y514-Y515, F540-Y544-F601, Y544-Y629, Y547-F551-Y629, F603-Y629, W657-W660, W676-W677, W712-W715
cation- π interaction	<6.0 Å	W386-K664, R392-Y675, H438-R490, R684-W703
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, Q276-Y323, F311-M372, P322-Y323, Y343-P377, F330-V691, W333-P726, P337-W712, W351-R684, M404-W509, H438-V410, Y471-L475/L534, R490-Y497, L555-Y590, R617-F618, V630-F634, L688-W703
Lone pair- π interaction	3-3.7 Å	Q276-F319, F395-C399, F405-V409, F476-N511, Y629-T633, W677-C678

Table S5. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 2-APB-PBC-activated state 2 of rTRPV2 in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID: 9B3V).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	D344-R702
H-bond	<3.9 Å donor-H-acceptor <60°	V254/M255/A257-K307, S291-G295, N292-Q294-K304, N292-L296, K300-N354 , A303/K304-C364, G306-N368, R317-S327/R328/K329, F319-S327, G321-Q324-S327, Y323-S327, P325/S327-R702, R328-D344, T331-C334, R339-E709, S341-Y343, D344-S346, D349-K385, I360/A361-R369, S366-N368, Q383-K661, K385-E672, Y403-Q479-T483, V410-Q414-H438/Y497, L434-H438, Q452-E473, S486-Y497, Y514-R517/S667, T516-T522, R517-W660, D536-R539, Y544-T604/Y629, E561-R617, E599-K602, L600-Y629, Q613-Q615, H651-A652, Y675-R679, R706-E708, N711-A714, W715-T718
π - π interaction	2.65–6.5 Å	W333-Y335, W351-W703, F362-Y455, W386-F393-Y515, F393-D394, F394/F397-F519, F397-Y515, Y400-Y403-F407, Y400-F476, Y400-Y515, Y412-H413, Y447-Y675/W676, W454-W457/W676, Y455-F456, Y471-F472-Y514, F476-Y514/Y515, Y514-Y515, Y544-F601, F547-F551, F551-Y629, F603-Y629, W657-W660, W676-W677-Y675, W712-W715
cation- π interaction	<6.0 Å	W386-K664, F362-R459, H438-R490
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, Y271-I314, F311-L315, F330-V691, W333-V340, P337-W712/W715, Y343-P377, W351-R684, A361-F362, W386-V390, M404-W509, F407-I441/L505, V410-H438, Y455-R459, F519-H521, F540-Y544/M640, V543-F547, F612-R619, R617-F618, V630-Y634, W657-K661, W660-K664, R684/L688-W703
Lone pair- π interaction	3-3.7 Å	H370-N655, Y455-E473, F476-N511, F476-PE-Y515, F601-T604, Y629-T633